

the application and are set forth in the Appendix A. Reconsideration of the application is requested.

### **Rejections Under 35USC §103**

Claims 1-21 are rejected as unpatentable over Hattersley *et al* taken with Nevo *et al*. The Examiner contends that Hattersley *et al* teaches compositions comprising BMP-2 and other growth and differentiation factors useful in methods of repairing articular cartilage and inducing cartilage formation, citing col. 1, lines 9-24; col.2, lines 30-63; col. 3, lines 2-31; and col.4 line 50 - col. 5, line 4. Applicants however point out that the disclosure at col.1, lines 9-24 and col.2, lines 30-63 is directed to BMP-2 in combination with PTHrP for induction and maintenance of cartilaginous tissue such as articular cartilage. Col. 3, lines 2-31 merely describes the TGF- $\beta$  superfamily. Applicants note that the sentence preceding col. 3, line 2 disclose the Hattersley *et al* method and composition again as a combination of a TGF- $\beta$  superfamily member and one or more parathyroid hormone-related peptides. It is Applicants understanding that the disclosure at col. 4, line 50 through col. 5, line 4 is directed to matrices and applications of the method and composition. Therefore, unlike Applicants invention the Hattersley *et al* disclosure requires parathyroid hormone.

The Examiner cites Nevo *et al* for teaching compositions for repairing damaged cartilage which include chondrocytes and other growth factors. The Examiner further states that Nevo *et al* teaches osteochondral grafting in repairing damaged cartilage. The Examiner thus concludes that where Hattersley *et al* teaches chondrocytes as a tissue source in cartilage development, it would have been obvious to one skilled in the art to have modified Hattersley *et al* by using the early teachings of Nevo *et al* to further support chondrocytes as a tissue source, as well as osteochondral grafts. Applicants submit that neither of the references alone or in combination teach Applicants' claimed invention, namely methods and compositions for the regeneration of articular cartilage comprising a BMP or BMP in combination with a tissue source. If one were to combine Hattersley *et al* with Nevo *et al*, the PTH requirement of the Hattersley *et al* composition is present.

Applicants request reconsideration and withdrawal of the finality of the rejection. The examiner contends that Applicants' amendments necessitated the new grounds of rejection. Applicants' amendments, however, were responsive to the previous rejection merely reciting the amount of the composition and duration of administration. In addition, the newly added claims were dependent from original claim 2 or 9 by further describing various "tissue sources" - an element already present in original claims 2 and 9 and yet the present rejection also applies to claim 2 and 9. Therefore, Applicants submit that the finality of the rejection ought be withdrawn.

Reconsideration of the application and entry of the amendments is requested. Should the Examiner believe that a telephonic interview would assist in clarifying any remaining issues, the Examiner is invited to call the undersigned attorney at the telephone number provided below.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Calims 8, 9 and 12 have been amended as follows:

(amended)8. A composition for regeneration of articular cartilage comprising ~~administering to an area in need of regeneration of said articular cartilage~~ an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.

(amended)9. A composition for regeneration of articular cartilage comprising ~~administering to an area in need of regeneration of said articular cartilage~~ an effective amount of a tissue source in combination with an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.

(amended)12. A composition for regeneration of articular cartilage comprising ~~administering to an area in need of regeneration of said articular cartilage~~ an effective amount of at least one purified protein selected from the group consisting of Vgr-2, growth and differentiation factors (GDFs), and bone formation-inducing protein(BIP) effective for the regeneration of said articular cartilage.

## Appendix A

1. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
2. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of a tissue source in combination with an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
3. The method of claim 1 wherein said BMP is BMP-2
4. The method of claim 2 wherein said BMP is BMP-2.
5. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified protein selected from the group consisting of Vgr-2, growth and differentiation factors (GDFs), and bone formation-inducing protein( BIP) effective for the regeneration of said articular cartilage.
6. The method of claim 1 further comprising a protein which induces the formation of tendon or ligament-like tissue.
7. The method of claim 6 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13 members of the BMP-12 subfamily and MP52.
8. A composition for regeneration of articular cartilage comprising an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration

of said articular cartilage.

9. A composition for regeneration of articular cartilage comprising an effective amount of a tissue source in combination with an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
10. The composition of claim 1 wherein said BMP is BMP-2.
11. The composition of claim 2 wherein said BMP is BMP-2.
12. A composition for regeneration of articular cartilage comprising an effective amount of at least one purified protein selected from the group consisting of Vgr-2, growth and differentiation factors (GDFs), and bone formation-inducing protein(BIP) effective for the regeneration of said articular cartilage.
13. The composition of claim 1 further comprising a protein which induces the formation of tendon or ligament-like tissue.
14. The composition of claim 6 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13 members of the BMP-12 subfamily and MP52.
15. The method of claim 2 wherein said suitable tissue source is osteochondral graft.
16. The method of claim 15 wherein said osteochondral graft is osteochondral allograft.
17. The method of claim 15 wherein said osteochondral graft is osteochondral autograft.
18. The composition of claim 9 wherein said suitable tissue source is osteochondral graft.
19. The composition of claim 18 wherein said osteochondral graft is osteochondral

allograft.

20. The composition of claim 18 wherein said osteochondral graft is osteochondral autograft.

21. A composition for the regeneration of articular cartilage said composition comprising an effective amount of a n osteochondral graft in combination with an effective amount of BMP-2 effective for the regeneration of said articular cartilage.